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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/577,943	05/03/2006	Daniel C. Carter	P07931US06/BAS	5248
881 7590 11/12/2009 STITES & HARBISON PLLC 1199 NORTH FAIRFAX STREET SUITE 900 ALEXANDRIA, VA 22314			EXAMINER BORIN, MICHAEL L	
			ART UNIT 1631	PAPER NUMBER
			MAIL DATE 11/12/2009	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/577,943

Applicant(s)

CARTER ET AL.

Examiner

Michael Borin

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 July 2009.
2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3, 6-9 and 13-35 is/are pending in the application.
4a) Of the above claim(s) 6-9, 13-35 is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 1-3 and 35 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SI/08)
Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____

DETAILED ACTION

Status of Claims

1. Amendment filed 07/14/2009 is acknowledged. Claims 4,5,12 are canceled. Claims 1-3,6-9,13-35 are pending. Claims 6-9, 13-34 remain withdrawn from further consideration. Claims 1-3, 35 are under consideration.

Abstract

2. The abstract of the invention is not descriptive. The abstract do not reflect the elected invention. A new abstract is required which are clearly indicative of the invention to which the elected claims are directed. An abstract on a separate sheet is required.

Abstract submitted 07/14/2009 is noted; however, the Abstract does not reflect the elected invention.

Specification Objections

3. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o).

Specification does not disclose region IIIA as claimed. See p. 11, lines 6-11. For example, residues at positions 422,445,450,452,490,492 addressed in the claims (claim 10) are not in the disclosure.

Applicant now points at Table III as demonstrating region IIIA as claimed; assuming that Table 3 is meant, said Table 3 presents residues surrounding binding sites, rather than residues of the binding site itself.

Claim Rejections - 35 USC § 112, second paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-3, 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection is applied for the following reasons.
 - A. Claim 1, step b), is directed to determining structural coordinates at the positions set forth in Table III. A assuming that Table 3 is meant, said Table 3 presents residues surrounding binding sites, rather than residues of the binding site itself. Therefore, it is not clear which "positions set forth in Table III" are meant as positions of the binding region. For the purposes of further analysis reference to particular positions set forth in Table III is disregarded.

Response to arguments

Applicant submits, first, that Table S1, referred to in original claims, was inadvertently addressed as "S1". This is surprising, as Table S1 is addressed on multiple occasions in the specification – see pages 9, 11, for example. Further, applicant submits that reference to Table S1 should be substituted with Table III. This is further confusing as

Table 3 presents residues surrounding binding sites, rather than residues of the binding site itself.

B. Claim 1b): This claim step addresses “model of association” between a putative binding compound and albumin binding region. However, the claim, in general, is directed merely to evaluating the ability of a compound to associate; there is no assertion that a random compound selected per claim 1a, for example by assembling random molecular fragments, will have an ability to associate. Therefore, it is not clear how the method step 1b) constructs a model of association which might not exist. Further, it is unclear how to create a model with precision ($< 3\text{\AA}$) required by the claim.

C. Claim 1b): The phrase “coordinates of the compound to albumin” is not clear. Is it coordinates of compound itself, coordinates of the compound in the vicinity of albumin coordinates of a complex with albumin?

D. Claim 1b). The phrase “binding coordinates” is not clear. The claim addresses “binding coordinates” of both “albumin binding region” and of the “compound”. It is not clear how to arrive at coordinates that are “binding”, especially considering that the method does not require the interacting molecules to bind, but is rather directed, loosely, to their ability to associate. Further, will the “binding coordinates” of residues of subdomain IB now defined at the end of claim 1, be the same when said defined subdomain is a part of another molecule or molecular complex (as addressed in the preamble of the claim)?

E. Claim 1c) addresses computer models_s in plural. It is not clear what plurality of models is being addressed if the preceding step 1b) addressed constructing a single model.

F. Claim 1c): Language “fitting program operation ... to be evaluated” is not clear. It is further not clear how evaluation of a fitting program would provide the intended result of “energy-minimized configuration”.

F. Claim 35: The phrase “compound is a compound binding to the IB subdomain as shown in Tables 1 or Table 2” is not clear. Does the reference to Tables 1,2 indicates the name of compound, the residues to be interacted with, etc., and how it defines the metes and bounds of the compound addressed in said claim 7?

If the amended claim language is intended to indicate the names of compounds present in Table 1, then the objective of the claim is not clear as the compound that has the ability to associate with the subdomain of interest is already identified.

If the amended claim language is intended to indicate coordinates to which the binding is to be determined, there are 26 instances of addressing domain IB in Table 2; in each instance, the set of residues varies – for example, the last two instances, p. 22, penultimate example has residues at positions L182, L185, not required for the last example. Contrary, the last example addresses, in part, residues at positions 135,139,158,193, not required in the preceding case. Thus, it is not possible to identify use of which coordinates is being addressed.

The following is a quotation of the 35 U.S.C. § 101:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

5. Claims 1-3, 35 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The instant claims are drawn to a computational method of evaluation of ability of compounds to "associate" with a protein subdomain. No physical transformation is addressed in the claims. Nor there is any recitation of a tie to another category of invention (the step of "constructing a computer model" is not viewed as necessarily involving use of a computer).

To qualify as a statutory process, the claims should positively recite the other statutory class (the thing or product) to which it is tied, for example by identifying the apparatus that accomplishes the method steps, or positively recite the subject matter that is being transformed, for example by identifying the material that is being changed to a different state or thing. In the instant case, claims do not recite any physical transformation step. Further, there is no step in the claims that recites a tie to another category of invention. Therefore, the claims are drawn to non-statutory subject matter for failing to recite a step that ties the method to another category of invention.

Further, there is no practical application to produce a real-world result as a result of the method as claimed. A tangible result requires that the claim must set forth a

practical application to produce a real-world result. In the instant case, there is no tangible output of a result of the claimed method.

Amendment of the claim to require, for step c), use of "computer or other apparatus" does not obviate the rejection. Such language does not require a tie to a particular machine, e.g., a computer sufficiently programmed to perform a particular fitting program, or other specific operation, and the claim reads on a mental activity (assuming that a human being can be seen as "apparatus").

Claim Rejections - 35 USC § 112, first paragraph.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-3, 35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are directed to determining structural coordinates with the root mean square deviation of not more than 3.0 angstroms from coordinates at the positions as in Table III; however, Table 3 (assuming the this table is meant as Table III) presents residues surrounding binding sites, rather than residues of the binding site itself.

Claim Rejections - 35 USC § 103.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 1-3,35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carter (US patent 5780594; reference provided by applicant) in view of Colmenarejo (Medicinal Research Reviews, Vol. 23, No. 3, 275-301, 2003; reference provided by applicant) and Floriano (US 2002/0099506).

Carter (the inventor of the instant invention as well) provides structural information on albumin subdomains obtained from crystallographic means (col. 3, last full paragraph). Carter teaches that albumin subdomain IIIA is one of albumin subdomains primarily responsible for binding properties of serum albumin (col. 2, last paragraph) and that the binding cavity in domain IIIA "the most active and accommodating on the human serum albumin, and many ligands have been found to preferentially bind in this region" (col. 4, first paragraph).

Carter does not teach use of computer modeling to identify "ability of compounds to associate) with albumin or its complexes as instantly claimed.

Floriano et al teach method of computer modeling to predict ligand-protein interactions wherein a binding region of the protein is identified using the structural information for the protein, and computer modeling is used to identify plurality of preferred binding conformations for potential ligands the preferred binding conformations are optimized using annealing molecular dynamics technique and the ligands with the lowest calculated binding energy in the optimized preferred binding conformations are selected. See claims 1-8.

Colmenarejo teach *in silico* methods for prediction of drug-binding strengths to human serum albumin (see Abstract).

In *KSR Int'l v. Teleflex*, the Supreme Court, in rejecting the rigid application of the teaching, suggestion, and motivation test by the Federal Circuit, indicated that

The principles underlying [earlier] cases are instructive when the question is whether a patent claiming the combination of elements of prior art is obvious. When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability.

KSR Int'l v. Teleflex Inc., 127 S. Ct. 1727, 1740 (2007).

Applying the KSR standard of obviousness to Carter and Floriano, Examiner concludes that the nature of the problem to be solved – evaluating potential of compounds to associate with albumin may lead inventors to look at references relating to possible solutions to that problem. Therefore, given the importance of the particular subdomain IIIA of albumin as being known as primarily responsible for binding

properties of serum albumin, and given the developing use of computational techniques to drug-binding strengths to human serum albumin, it would have been obvious to use computational methods of Floriano for modeling ligand-protein interactions to identify ligands that interact with this particular albumin subdomain.

With respect to claims 10,12, Carter teach that binding region IIIA spans between residues 375 and 495 (col. 4, last paragraph). Thus, a three dimensional model would include all of the residues as instantly addressed, and it would be obvious to an artisan to select particular residues of interest.

Response to arguments

Applicant arguments were considered but are not deemed persuasive. Applicant seems to argue that the instant method provides "a more accurate predictive tool". There are no method steps distinguishing the instant method from the cited prior art; nor there is a demonstration of unexpected results in specification. Further, applicant argues that the method allows accurate prediction of the placement of drug. First, it is not evident that the existing methods provide inaccurate predictions. Second, with respect to "exact placement", the amended claims are confusing as they rely on Table 3 which addresses residues surrounding residues of the binding site, rather than the residues of the binding site itself.

Further, applicant argues that Colmenarejo is not a prior art. Colmenarejo was published online Jan 28 2003 (as stated on the Journal's web site,

<http://www3.interscience.wiley.com/journal/102525257/issue>) which predates the effective filing date of the instant application.

Conclusion.

8. No claims are allowed
9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. The examiner can normally be reached on 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael Borin, Ph.D./
Primary Examiner, Art Unit 1631

mlb